Medical and Pediatric Oncology 27:160–164 (1996)

Outcome of Children Treated for Cancer in the Republic of Namibia

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The data of a survey undertaken to record all cases of childhood cancer in Namibia from 1983 to 1988 were analyzed to estimate 5-year survival rates. The projected survival rate for 150 children with cancer was 37% with no difference between boys and girls. The calculated survival rates for most of the tumor groups were poor with the exception of Wilms' tumor which had a 5-year survival rate of 76%. The zero survival rate of children with malignant bone disease may have been due to inadequate treatment. Neuroblastoma and retinoblastoma presented with advanced disease which contributed to the poor survival rates of 13% and 46%, respectively. The overall survival rate for lymphoma of 53% and 39% for all leukemias compares poorly with the rates obtained in industrialized countries. The relatively poor 25% survival rate in tumors of the central nervous system (CNS) may partly be due to the long delay between the initial diagnosis and the institution of appropriate treatment for raised intracranial pressure and for the tumor.

Both cure and long-term follow-up are difficult to achieve in a developing country. Improved early diagnosis and appropriate treatment are necessary to improve survival rates.

Key words: Namibia, survival, childhood, cancer, registry

INTRODUCTION

Survival rates in children with cancer in Africa are largely speculative at present. Some countries and institutions in Africa have reported survival rates for individual tumor groups such as Wilms' tumor, Hodgkin's disease and Burkitt's Lymphoma [1–3]. These reports often do not include long-term follow-up and the survival rates were not always calculated by actuarial methods. An estimate of survival in children with cancer from a registry which is based on national population data, has to our best knowledge not been published for an African country.

The calculated survival rates of all children diagnosed with cancer in Namibia between January 1983 and December 1988 are reported in this paper.

METHODS

A survey was undertaken to record all cases of pediatric cancer in Namibia during the 6-year period from January 1983 to December 1988. Details of children treated at the pediatric cancer unit (PCU) at Tygerberg Hospital (TBH) in the Republic of South Africa (RSA) had been recorded in the childrens' tumor registry of that hospital. Records of all district, central, and referral hospitals, and death certificates as well as the complete records of the central pathology service in Namibia were scrutinized to ensure maximal ascertainment of patients for the study period. Any child resident in Namibia during the survey who was less than 15 years of age and in whom any malignant neoplasm, intracranial tumor or histiocytosis was diagnosed, was recorded. Information for 118 patients was available from the hospital registry at TBH. An additional 45 new patients were identified with the methods outlined above. Diagnosis and staging of tumors were based on histological, laboratory, and clinical investigations. The patients were classified according to the scheme proposed by Birch and Marsden [4].

Survival was analyzed 1 year after the survey closed. The incidence date, or if that was unknown, the date of diagnosis, was used as the entrance date in the analyses. Survival was calculated by actuarial methods as described by Kaplan and Meier [5]. Confidence intervals (CI) were calculated according to Greenwood's formula [6]. A child was eligible for inclusion in the analysis irrespective whether or not treatment for the cancer had been given. Survival was analyzed for 150 out of 163 patients recorded during the survey. Three patients with germ cell tumors, two with a renal tumor, as well as one each with a brain tumor, a soft tissue sarcoma, and an unclassified orbital tumor were excluded from analysis because of insufficient data. A further 4 skin tumors and 1 case of

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Received March 16, 1995; accepted December 11, 1995.

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histiocytosis were excluded because we considered these to be either locally invasive or a nonmalignant condition. Because of small numbers, patients with different types of leukemia, lymphoma, brain tumors, malignant bone tumors, and soft tissue sarcomas were not subdivided when calculating survival.

The majority of children were treated according to standard treatment regimens under the supervision of the pediatric cancer unit at Tygerberg Hospital in the Republic of South Africa. The treatment of malignant bone tumors was a notable exception, as these children were primarily treated surgically in other departments and only a few received limited chemotherapy. The BFM 83 [7,8] protocols were used for the treatment of the leukemias, chlorambucil, vinblastine, procarbazine, and prednisolone with low dose involved field radiotherapy [9] in Hodgkin's disease, LSA_2L_2 [10] in lymphoblastic lymphoma, cyclophosphamide, oncovin, methotrexate, and prednisone [10] in B-cell and other non-Hodgkin lymphomas, surgery, and radiotherapy for brain tumors, NWTS 3 [11] in Wilms' tumor, and a St. Jude protocol [12] in neuroblastoma.

On completion of treatment, the frequency of follow-up visits was determined by the type of tumor. Regular follow-up visits were managed by pediatricians at Windhoek State Hospital and at Oshakati Hospital in Namibia. Children treated at the PCU at TBH returned to South Africa only when special investigations or modalities, which at the time were unavailable in Namibia, e.g., computed tomography, were required during follow-up. Regular contact by telex, telephone, or mail between the authors and medical and nursing staff or social workers at the Windhoek State Hospital and the regional hospitals ensured frequent update concerning the majority of patients. A regular 6-month inquiry was made to ascertain the health status of those patients who had missed follow-up appointments or no longer presented themselves for regular follow-up visits. To establish outcome in patients diagnosed retrospectively during the survey, the help of regional health workers such as general practitioners, nurses and social workers was enlisted. The regional radio services and public notices at district clinics were used in an effort to trace these patients.

RESULTS

Of the 163 patients recorded during the survey, 88 were male (mean age 6.9 years) and 75 female (mean age 7.5 years). One hundred and thirty-seven were of African ethnic origin and 26 were of European or mixed ethnic origin. The overall incidence of pediatric cancer (children < 15 years of age) in Namibia during the study was 55.5 per million children. The incidence rate was calculated by using the population figures and growth rates reported by the 1981 national census of Namibia [13]. The distribution, deaths, and projected 5-year survival of the main diagnostic groups are shown in Table I. Ninety-one percent of these diagnoses were confirmed histologically and in an additional 6% of patients, brain tumors were diagnosed with the aid of computed tomography. Two patients with leukemia were diagnosed on a peripheral blood smear and 2 patients with neuroblastoma who presented with extensive disease, were diagnosed clinically and died soon after admission.

The calculated survival for the 150 tumors analyzed was 37% with a confidence interval of 26–47%, and is shown in Figure 1. At the time of analysis, 41 patients were known to be alive, 81 had died, and 28 were censored because of loss to follow-up. There was no difference in the 40% survival (CI 27–53) in boys and 30% survival (CI 11–48) in girls. The survival rates for the major diagnostic tumor groups are illustrated in Table I. The projected 5-year survival rate for malignant bone tumors and soft tissue sarcomas (STS) was 0%. The rates for tumors of the central and sympathetic nervous system were 25% and 13%, respectively. The 76% survival rate of patients with renal tumors was significantly better than the aforementioned malignancies. The projected survival rates of all the leukemias and all the lymphomas were 39% and 53%, respectively, with a rate of 42% for the non-Hodgkin lymphomas.

DISCUSSION

The analysis of the survival data as at December 1989 was performed 7 years after the start of the survey and 1 year after the last patient had been entered in the study. At that stage, 74 (45%) of the 163 recorded patients were known to have died of tumor-related causes, 41 (25%) were alive and disease-free, 28 (17%) had been lost to follow-up, 7 (4%) had died of tumor-unrelated causes, and 13 (8%) patients could not be included in the survival analysis, due to insufficient data or for reasons stated above. A comparison of survival rates for Namibia, the USA, and the UK is provided in Table II [14,15]. The value of the calculated survival rates for Namibian children is limited by the small number of tumors and the resultant wide CI. The wide CIs make a statistical comparison with other survival figures unreliable. The survival rates were nevertheless calculated and compared with rates in other countries to contribute to the limited available data on survival rates for children in African countries and secondly, to assess efficacy of treatment at the time of the survey. The precision of survival rates could further be adversely influenced by the fact that a considerable number of patients were lost to follow-up and therefore censored from the Kaplan Meier survival analysis. At the time of analysis, 40% of the patients who had not suffered a final event (28 out of 69), had been lost to further follow-up. Incomplete follow-up of cancer pa-

TABLE I. Distribution Deaths and 5-Year Actuarial Survival of the Main Diagnostic Groups

Diagnostic group	Total number	Number analysed	Deaths	5-Year % survival	CI(%)[b]
Leukemias	19	19	11	39	15–63
Lymphomas	19	18	9	53	30–77
Central nervous system	28	27	16	25	3–47
Sympathetic nervous system	14	14	11	13	2–37
Retinoblastoma	16	15	8	46	18–73
Renal tumors	21	19	6	76	56–92
Liver tumors	1	1	1	NC[a]	—
Bone tumors	15	15	6	0	0
Soft tissue sarcomas	16	15	8	0	0
Gonadal and germ cell	3	0	0	NC	—
Epithelial neoplasms	4	4	4	NC	—
Other	7	3	1	NC	—
Total	163	150	81	37	26–47

[a]NC, Group survival not calculated.
[b]CI, Confidence interval.

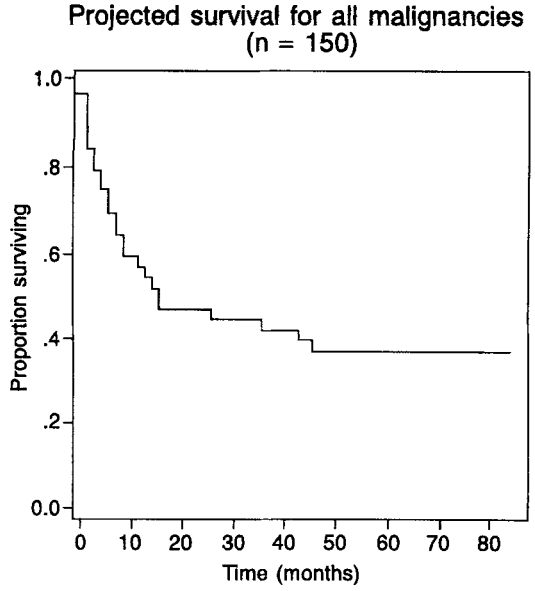

Fig. 1. The outcome of children treated for cancer in the Republic Namibia.

TABLE II. Calculated Survival Rates (%) for Cancer in Children From Namibia and Other Countries

Diagnostic group	Country		
	Namibia	USA[a]	UK[b]
Leukemias	39	51	70
Non-Hodgkin lymphomas	42	51	70
Brain and spinal cord	25	52	45–72[c]
Sympathetic nervous system	13	50	43
Retinoblastoma	46	88	85
Renal tumors	76	76	79
Bone tumors	0	48	42–54[c]
Soft tissue sarcomas	54	58	61
Overall survival	37	57	NR[d]

[a]Reference 14: 5-year survival, data for 1973–1981.
[b]Reference 15: 5-year survival, data for 1983–1985.
[c]Survival reported for subgroups of main diagnostic group.
[d]NR, Not reported.

tients is a problem in many developing countries. Strategies to improve follow-up of patients in Namibia and other developing countries are urgently needed to ensure continuous and complete treatment and to allow accurate assessment of survival.

The incidence rate of 55 per million recorded in Namibia is approximately half that of the USA and other African countries such as Nigeria and Uganda [14,16]. The Namibian incidence rate suggests that pediatric cancer in Namibia may have been underascertained by 50%. Completeness of ascertainment was, however, difficult to evaluate with conventional methods, as death certificates are not available or mandatory in many areas; no national cancer registry or reporting system existed and this was the first survey of its kind in Namibia [17–19]. Ninety-one percent of cancers were confirmed histologically and an additional 6% were brain tumors diagnosed by computed tomography. These figures suggest that a high degree of diagnostic accuracy was achieved during the survey.

The 5-year survival rate in Namibian children is compared with the rates reported for American and British children in Table II. The 37% survival rate is worse than the 57% overall survival in children who were treated in the USA between 1973 and 1981 [14]. The rates reported by this USA study are relative survival rates. This rate was used for comparison with the observed Namibian rates as the difference between relative and observed survival rates in children is small. The rates reported from the UK are for children treated between 1983 and 1985 and illustrate what can be achieved with modern treatment

[15]. Children from Namibia fared worse for all categories of tumors except for Wilms' tumor (WT) with a calculated 5-year survival rate of 76% (Table I). Due to the few recorded tumors, the CI for this survival rate ranges from 56% to 97%. Wilm's tumor, however, remains the only tumor in Namibian children that has a survival rate comparable to those reported in developed countries. Nkrumah achieved encouraging results in the treatment of WT in Zimbabwe by using vincristine sulphate and D-actinomycin in combination with radiotherapy, after resection of the tumor [1]. Fifty-six percent of the tumors in the Zimbabwean children were stage III, IV, or V and the overall survival rate at 2 years was 65%. Fifty-three percent of the WTs in this Namibian survey were either stage III or IV disease and the projected survival for all WTs at 1, 3, and 5 years was 82%, 76% and 76%, respectively. The Namibian children were treated according to the National Wilms' Tumor Study III protocol [11]. It is difficult to explain the good results obtained in the treatment of WT in Namibia in comparison with the other tumor groups. Perhaps the relatively slow progression of the WT, the often visible external disfigurement or the easily palpable mass in a young child enabled parents to bring these children for medical care.

The calculated 5-year survival rate of 39% (CI 15%–63%) for leukemia compares poorly with survival currently obtained in the UK [20]. A poor prognosis in developing countries and in black African children with leukemia has been previously documented [21–23]. Fifteen (80%) of the Namibian children in this study were black. The inclusion in the analysis of 3 cases of acute nonlymphocytic leukemia and 1 patient with acute lymphoblastic leukemia (ALL) aged less than 1 year may have negatively influenced the survival rate in Namibian children. If these 4 patients are taken into consideration, the overall survival rate in leukemia of 39% is an encouraging result for a developing country. All the children with ALL were treated with the BFM 1983 medium risk protocol [7].

The poor outcome of brain tumors (25% survival) may partly be due to the long delay between the making of the provisional diagnosis of a brain tumor with raised intracranial pressure, and the initiation of definitive treatment. All children with brain tumors were referred to Tygerberg Hospital in the RSA for surgery and radiotherapy during this survey. The average delay in 11 patients between the time of diagnosis and the provision of a shunt for raised intracranial pressure was 24 days. In 3 other patients, available information suggested delays of 3, 9 and 18 months, respectively, before the onset of therapy. Such delays, which influence morbidity and mortality, could be reduced by initiating treatment (e.g., a shunting procedure) in Namibia. The majority of brain tumors [9] were astrocytomas. There were 8 other gliomas, 3 medulloblastomas, 1 ependymoma, and 7 tumors classified as other.

All the children with neuroblastoma (NB) had advanced disease at diagnosis. There were 4 children with Evans stage III and 10 children with stage IV NB. Three of the 14 children were less than 1 year old at diagnosis. One of these infants is alive and disease-free, 1 died of a nontumor-related cause and the third died as a result of NB. The poor survival of Namibian children with NB is probably a reflection of advanced disease and the relatively few patients who are less than one year of age at diagnosis. A high incidence of advanced disease at diagnosis in black South African children has also been reported by Hesseling et al. [22].

Retinoblastoma (RB) has an excellent prognosis in developed countries and survival rates of 85% to 88% have been reported for British and American children [14,15]. The good prognosis is related to early detection and adequate treatment of the tumor. In contrast, the results obtained in developing countries, and specifically Africa, are poor [24]. Only 5 out of 48 patients with RB in Zaire were alive 3 years after diagnosis [25]. In Namibian children, the calculated 5-year survival rate of 46% (CI 18%–74%) was approximately half the rate reported in developed countries. The majority of RB patients in this series had advanced disease at diagnosis which necessitated enucleation followed by radiotherapy and additional chemotherapy. The average delay of 3.5 months between diagnosis and referral for treatment may have contributed to the presence of extensive disease at the onset of treatment. Personnel involved in primary health care need to be taught the early signs of RB, such as the loss of the red reflex in an eye or the development of a squint, and the importance of early referral of these children.

The survival figure for malignant bone tumors in Table I does not distinguish between osteosarcoma and Ewing's sarcoma. No Namibian child with a malignant bone tumor (MBT) survived, in contrast to an expected cure rate of around 50% in developed countries [14,15]. This poor result is probably due to inadequate treatment, as 14 out of the 15 children with MBT were primarily treated surgically and only a few patients received additional chemotherapy which consisted of only 2 to 3 courses of adriamycin or cis-platinum. Only a few soft tissue sarcomas were available for analysis. A late death resulted in the prediction of a 0% survival for soft tissue sarcomas.

The survival rates of Namibian children with cancer are generally poor. The rate for patients with WT, however, indicates that it is possible to attain results equal to those of developed countries. Survival rates for leukemias and lymphomas were approximately 50% of the rates reported by developed countries. The results are nevertheless encouraging because they prove that long-term cure and follow-up for some patients can be achieved in a developing country. At present, all Namibian pediatric cancer cases are primarily treated in Windhoek and only compli-

cated cases or those requiring radiotherapy are referred to TBH. The treatment regimens used are those presently utilised by the PCU at TBH and there are regular consultations between the treating physicians of the 2 institutions.

ACKNOWLEDGMENTS

The authors thank the various health workers in Namibia for their help and the Harry Crossly and Yvette Naude Funds for financial support to undertake this survey.

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